

SUPPORT FOR THE AMENDMENT

Support for the amendment to claims 18-19 is found on page 12, lines 18-21 of the specification.

No new matter would be added to this application by entry of this amendment.

Upon entry of this amendment, claims 1, 3-5 and 7-19 will remain active in this application.

REQUEST FOR RECONSIDERATION

The claimed invention is directed to a process for preparing a treated immobilized enzyme.

Applicants wish to thank examiners Fernandez and Lankford for the helpful and courteous discussion held with their U.S. representative on June 21, 2006. At that time, applicants U.S. representative argued that the evidence of record restricted the meaning of the term "consisting essentially of" to exclude the presence of a reactive alcohol with fatty acid and enzyme. In addition, applicants' U.S. representative argued that an amount of substrate of 800 to 5,000 wt. % was not suggested by the generic teaching of the references, a final water content of 5-50 wt. % was achieved when using the claimed contact amount as compared with using the 400 wt. % exemplified in the reference and there was no motivation to use a reaction amount of substrate in the treating step of Shimizu et al U.S. '610. The following is intended to expand upon the discussion with the examiners.

The use of immobilized enzymes for the decomposition of oils and fats has become of increased interest based on the discovery that partial glyceride compositions may provide advantageous health effects. Dried immobilized enzymes have been used however can suffer from a loss of activity. Improved methods based on contacting an immobilized enzyme with

a reaction substrate, without drying in order to carry out an esterification reaction have been reported. Such methods have been described as providing high activity of the enzyme on and after the second reaction (page 2, lines 12-16 of applicants' specification). However, methods of preparing a treated immobilized enzyme of high activity can still be improved upon.

The claimed invention addresses this problem by providing a method for preparing a treated immobilized enzyme in which A) an immobilized enzyme is brought into contact, without drying, with 800-5,000% by weight of a fatty acid triglyceride, partial glyceride or mixtures thereof to provide a moisture content of from 5-50% by weight (claims 1 and 5); or B) contacting an immobilized enzyme, without directly drying, with a composition consisting essentially of a fatty acid, fatty acid triglyceride, fatty acid partial glyceride or mixtures thereof, followed by dehydration to a moisture content of 1-50% by weight based on the weight of the carrier (claims 3, 4 and 7). Applicants have discovered that both methods provide for an immobilized enzyme of high activity. Such methods are nowhere disclosed or suggested in the cited prior art of record.

Claims 3, 4, 7-8, 10, 12, 14, 16-17 and 19:

This embodiment of the claimed invention is directed to a method in which the immobilized enzyme is sequentially contacted with a composition **consisting essentially of** a fat or oil, then subject to a separate dehydration step.

The rejection of claims 3, 4, 7, 8, 10, 12, 14, 16, and 17 under 35 U.S.C. § 103(a) over Bosley et al U.S. 5,658,769 in light of Macrae et al EP 322,213 and in view of Ikuta et al U.S. 5,569,594 is respectfully traversed.

None of the cited references disclose or suggest preparing a treated immobilized enzyme by contacting the immobilized enzyme, without directly drying following

immobilization, with a composition consisting essentially of at least one of a fatty acid, a fatty acid triglyceride, a fatty acid partial glyceride or a mixture thereof.

Bosley et al. fails to describe contacting the immobilized enzyme, without directly drying following immobilization, with a composition consisting essentially of at least one of a fatty acid, a fatty acid triglyceride, a fatty acid partial glyceride or a mixture thereof. The examiner notes that Bosley et al. prefer using an immobilized enzyme such as prepared according to Macrae et al. EP 322,213 (pg 6 of official action). However, each and every example of immobilization of an enzyme according to Macrae et al. subjects the immobilized enzyme to **drying under vacuum** at room temperature. In Ikurta et al., the immobilized enzyme is dried, for example by drying under reduced pressure to a water content of desirably 0.5 to 30 wt.%. (column 3, line 65 through column 4, line 2). Thus, these references do not suggest contacting the immobilized enzyme, without directly drying following immobilization, with a composition consisting essentially of at least one of a fatty acid, a fatty acid triglyceride, a fatty acid partial glyceride or a mixture thereof.

In contrast, the invention of claims 3, 4, 7-8, 10, 12, 14, 16-17 and 19 is directed to a process in which, without directly drying after immobilization, the immobilized enzyme is brought into contact with a composition consisting essentially of at least one of a fatty acid, a fatty acid triglyceride, a fatty acid partial glyceride or a mixture thereof. Such a method is nowhere disclosed or suggested by the cited references.

The examiner notes on page 9 of the official action that the transitional phrase “consisting essentially of” has been interpreted by the examiner as “comprising” as the examiner has found “no evidence that any of the additional ingredients present in the prior art composition would affect the basic and novel properties of the prior art method such that the prior art method is truly different than the claimed method.”

Applicants respectfully submit that the examiner's characterization of the proper method of interpreting this claim term is somewhat misstated and that the transitional phrase "consisting essentially of" must be properly interpreted to exclude an alcohol which would undergo esterification with a fatty acid.

A clear indication of the basic and novel characteristics of the claimed invention is found in applicants' specification on page 1 as follows:

"The present invention relates to a process for preparing an immobilized enzyme showing a high activity. Such immobilized enzyme is used as a catalyst in the esterification of a fatty acid with an alcohol or transesterification of oil & fat."

Thus it is clear that the claimed invention is directed to a process in which 1) an immobilized enzyme of high activity is obtained; and 2) the enzyme of high activity may be used in esterification or transesterification reactions. With such a clear indication of what the basic and novel characteristics of the claimed invention are, it is improper for the examiner to construe this transitional phrase as "comprising." M.P.E.P. §2111.03.

While applicants have the burden of showing that the introduction of an alcohol which would undergo esterification would materially change the characteristics of applicants' invention (M.P.E.P. §211.03) of providing an immobilized enzyme showing high activity, such evidence is already of record.

Example I of Bosley et al. reacts oleic acid with *t*-butanol in the presence of an immobilized lipase to form *t*-butyl oleate. Applicants note that reaction of oleic acid with *t*-butanol in an esterification reaction is contrary to the basic and novel characteristics of the claimed invention of providing an immobilized enzyme having high activity in so far as use of the immobilized lipase to catalyze the reaction of oleic acid with *t*-butanol will reduce the activity of the immobilized lipase. That use of an immobilized lipase will contribute to a reduction in the activity of the enzyme is evidenced by Ikuta et al. cited by the examiner, in which example 18, at column 13 measures the "Duration of Life for the Immobilized

Enzyme”, in terms of maintenance of enzymatic activity as a result of use. As the duration of life is measured in terms of the time of use before deactivation, it is clear that use of the enzyme for its intended purpose will contribute to a reduced activity of the enzyme. As the goal of the claimed invention is to provide an immobilization method for an enzyme with high activity, the presence of a reaction substrate along with a fatty acid would clearly be contrary to such a goal and therefore applicants’ claim term of “consisting essentially of” excludes the presence of such an alcohol with a fatty acid and immobilized enzyme as claimed. Such a showing clearly meets the burden placed on applicants in contending that a reactive alcohol is excluded by the recitation of the transitional phrase “consisting essentially of.”

As none of the cited references disclose or suggest a method in which the immobilized enzyme is, without directly drying, contacted with a fatty acid, a fatty acid triglyceride or a fatty acid partial glyceride or mixture thereof, the claimed invention is clearly not made obvious from these references and withdrawal of the rejection under this section of the statute is respectfully requested.

Claims 1, 5, 9, 11, 13, 15 and 18:

This embodiment of the claimed invention is directed to a method in which an immobilized enzyme is, without drying, brought into contact with 800-5,000% by weight based on the weight of carrier of a fatty acid triglyceride, a fatty acid partial glyceride or mixtures thereof to provide a final moisture content of from 5-50% by weight based on the weight of the carrier.

The rejections of claims 1, 5, 9, 11, 13, 15 and 18 under 35 U.S.C. 103(a) over EP 1,008,647 in view of Shimizu et al U.S. 6,258,575 and Ruthven and over Shimizu et al. U.S. 6,716,610 or US 2003/0096383 are respectfully traversed.

None of the cited references disclose or suggest a contacting amount of 800-5,000 wt. % nor a moisture content of 5-50 wt.% after contacting with a oil/fat.

EP '647 fails to disclose or suggest a moisture content of 5-50 wt. % **based on the weight of the carrier** resulting from treatment of an immobilized enzyme with a fat/oil, without drying.

The examiner cites to Shimizu et al. U.S. 6,258,575 as making it obvious to use an amount of 4,100wt.% of oil, based on the weight of carrier, in the contacting step of EP '647.

Applicants respectfully submit that there is no motivation provided by Shimizu et al. U. S. '575 to use an amount of oil of from 800 to 5,000 wt. % in a contacting step of an immobilized enzyme, without drying, as the passage of Shimizu et al. U. S. '575 relied upon by the examiner describes an amount of oil used as a **reactant** in a hydrolysis reaction, not an amount of substrate used to treat an immobilized enzyme which has not been dried.

Example 2 of Shimizu et al. U. S. '575, cited by the examiner, reacts soybean oil with an immobilized lipase. The oil phase substrate is fed to the enzyme column 13 "to initiate the decomposition" (column 8, lines 45-47). Such a reaction is fundamentally different from the contacting to stabilize an immobilized enzyme for storage, as described by EP '647 (paragraph [0034]). One of ordinary skill in the art would not look to the amount of substrate to be reacted when determining an amount of substrate to contact with an immobilized enzyme as the fundamental purpose of the substrate is different in the two processes. In EP '647 the substrate is used to stabilize an immobilized enzyme for storage stability, while in Shimizu et al. U. S. '575, the substrate is used to produce a quantity of desired product. In Shimizu et al. U. S. '575, the amount of substrate which is used is determined by the amount of product desired.

In contrast, according to EP '647, after contacting, the substrate is filtered and the immobilized enzyme is recovered ¶[0034]. There would certainly be no motivation to use

more substrate than what was believed to be necessary since the substrate performs no value other than stabilization of the immobilized enzyme. Use of an excess of substrate in this step would simply be a waste of substrate. Why would you use more substrate than what was believed to be necessary? In using a greater amount of substrate for this treatment requires 1) more substrate; and 2) a larger reaction vessel; and 3) more energy to provide the desired contact temperature as a greater amount of substrate would need more energy to be heated (~60°C ¶[0034]). Thus, simple economic reasons would preclude any motivation to use more substrate than was believed to be necessary. As there is no guidance in EP '647 as to the amount of substrate to be used, the only example uses only 400 wt.% of substrate, and there are clearly economic motives not to use more material than is believed to be necessary, there is certainly no motivation to contact the immobilized enzyme of EP '647 with an amount of substrate in excess of 400 wt. % based on the carrier.

In addition, there is no suggestion to have a moisture content **after contacting** the immobilized enzyme with the oil/fat to be within a range of 5-50 wt.% based on the weight of the carrier.

The examiner cites to the disclosure of EP '647 which describes the water content of the immobilized enzyme of 20% or more by weight, preferably 40-60 wt.% **prior to contacting** with substrate ¶[0034]. However, this disclosure provides no guidance as to the water content **after** contact with the substrate. The examiner attempts to conclude and deduce based on teachings of 1) water should be removed from an esterification reaction using an immobilized enzyme; and 2) the water content of an immobilized enzyme prior to contacting with a substrate treatment is at least 20wt. %, or 40-60 wt. %, that an amount of water, **after treatment with the substrate**, should be from 5-50 wt. %. To the contrary, the reference's description of the water content prior to contact but not after contact, suggests that the water content after contact with the substrate is not important whatsoever. There is

no motivation to provide a moisture content of 5-50wt. % based on this disclosure. Clearly quantification of a variable at one point in time but not later would suggest that at the later time the variable is of no importance. For at least this reason, there would be no motivation to have the water content to be from 5-50 wt. %.

In the absence of any express disclosure of these two claim limitations, the examples may none the less provide some guidance as to any inherent disclosure as to these two claim limitations. However, example 1 of the reference only reacts 400 wt. % of oil, based on the weight of carrier and that treatment of immobilized enzyme with this amount of oil provided for a moisture content, based on the weight of carrier, of 66 wt.%. Therefore, the example does not provide any suggestion of the claim limitation of 1) contacting “with 800 to 5,000 wt.% of fatty acid triglyceride, a fatty acid partial glyceride or mixtures thereof” or 2) a moisture content of 5 to 50 wt. % based on the weight of carrier.

Example 1 of the reference is explained in further detail below.

According to example 1 of Shimizu et al. ‘610 and EP ‘647 an immobilized enzyme on 10 grams of carrier is treated with 40 grams of soybean oil. The ratio of the amount of fat/oil based on the carrier is 400%, **well below** the claimed 800 wt. % minimum. Applicants have previously submitted the declaration of Mr. Manabu Sato, a named inventor of the above-identified application. The Sato declaration prepared an immobilized enzyme, and, without drying, treated the enzyme with various weight percentages of oil. 400 wt. % was used as exemplary of Example 1 of Shimizu et al. ‘610. 800 and 1,000 wt. % were used as examples according to the present invention. For the Examiner’s convenience, the table from the Sato declaration is reproduced below.

	Example	Oil amount for contacting with the immobilized enzyme (wt.% based on weight of the carrier)	The amount of oil in the immobilized enzyme after filtration (wt.% based on weight of the carrier)	Moisture content	
				* (wt% based on the weight of the carrier)	** (wt% based on the weight of the immobilized enzyme)
US 6,716,610	Example 1	400	150	66	21
Claimed Invention	Newly measured data	500	150	52	17
		800	150	42	14
	Example 1	1000	150	29	11

As is apparent, at a treatment ratio of 400% as used in Example 1 of Shimizu et al. '610 and EP '647, the residual moisture content based on the carrier remains high at 66%, well in excess of the claimed range of 5-50 wt. %. In contrast, when treated with amounts of 800 and 1,000 wt.%, the residual moisture content based on the weight of carrier was much lower at 42 and 29 wt.%, respectively. Accordingly, by treatment with an amount of 800-5,000 wt.% of oil, a residual moisture content based on the weight of carrier of 5-50% by weight may be achieved. As the reference fails to disclose or suggest such an amount of oil, nor provides guidance as to a moisture content of 5-50 wt. %, based on the weight of carrier, the present invention is believed not made obvious from this reference.

To the contrary, applicants have demonstrated that both endpoints of the claimed range of 800 to 1,000 wt. % of oil provide for a residual moisture content within the claimed range of 1 to 50 wt. %, and that outside of the claimed range of 800 to 1,000 wt. % of oil, that a residual moisture content in excess of 50 wt.% is observed. Therefore, the claimed range of 800 to 1,000 wt.% of oil is not obvious based on the lower residual moisture content obtained, an amount much lower than the 66 wt. % obtained in the example of the reference.

Furthermore, any assertion that it would have been obvious to optimize the water content to be from 5-50 wt. % is simply not supported by the art of record.

There is no description of any relationship between the amount of water and any result and accordingly the water content can not be optimized to obtain any known result.

A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie* 195 USPQ 6, (CCPA 1977) (MPEP 2144.05(b))

Moreover, a moisture content within the claimed range is not inherent to the process of Shimizu et al. '647 as there is no teaching to use an amount of oil which would result in a moisture content as claimed.

Withdrawal of the rejections under 35 U.S.C. §103(a) are respectfully requested.

The rejection of claims 1, 5, 9 11 and 13-19 under 35 U.S.C. §112, second paragraph has been obviated by appropriate amendment.

Claims 1, 15 and 16 have been amended to clarify that the enzyme from the immobilization step i) is, without drying, brought into contact with a substrate and that the moisture content of the immobilized enzyme is as a result of the contacting step.

Claims 13-19 have been amended to recite that the amounts are based on the amount of carrier. As recognized by the examiner, these amounts are % by weight.

In view of applicants' amendments withdrawal of the rejections under 35 U.S.C. §112, second paragraph is respectfully requested.

The rejection of claims 1, 5, 9 and 13 under the judicially created doctrine of obvious-type double patenting over claims 1-4 of U.S. 6,716,610 is respectfully traversed.

None of the claims of U.S. '610 claim a contacting amount of 800-5,000 wt. % or a moisture content of 5-50 wt. %. Applicants have provided evidence that a contact amount below the claimed range (e.g. 400 wt. %) results in a moisture content in excess of the

claimed range (e.g. 66 wt. %). Since there is no teaching of the contact amount or the moisture content, there is no motivation to provide a contact amount of 500-8,000 wt. % or a moisture content of 5-50 wt. %. Thus, the claimed invention of claims 1, 5, 9 and 13 is not obvious over the claims of U.S. '610.

Applicants submit that this application is now in condition for allowance and early notification of such action is earnestly solicited.

Respectfully submitted,

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